UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,094	12/31/2003	Gautam Vinod Daftary	B2351010.1	6940

26158 7590 08/27/2008

WOMBLE CARLYLE SANDRIDGE & RICE, PLLC
ATTN: PATENT DOCKETING 32ND FLOOR
P.O. BOX 7037
ATLANTA, GA 30357-0037

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
08/27/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,094	DAFTARY ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,12,14-22 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,12,14-22 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 5-22-08is acknowledged.

Claims included in the prosecution are 1-8, 10, 12, 14-22 and 62.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-8, 10, 12, 14-22 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirpotin (6,110,491) in view of Papahadjopoulos (4,235,871).

Kirpotin discloses a method of preparation of liposomes by forming a lipid film and hydrating it with a buffer containing ammonium sulfate (Example 7). Kirpotin also teaches that if necessary, to achieve an osmolarity of 377 mmole/kg, sucrose could be added to the medium (Example 8). The liposomes contain hydrogenated egg phospholipid and cholesterol. Doxorubicin is loaded into the preformed liposomes (Example 7). Although in the examples Kirpotin uses PEG-phospholipids, on col. 9, lines 22-33 teaches either the naturally occurring or synthetic phospholipids which implies that the use of PEG-phospholipids for the method of preparation of liposomes is not necessary. What is lacking in Kirpotin is the teaching of the amount of aqueous

medium added to per mol phospholipid. However, since the final product in Kirpotin is a liposome just as in instant case and since complete hydration of the phospholipid is required for the formation of the liposomes, in the absence of showing unexpected results, it is deemed obvious to one of ordinary skill in the art to vary the amounts of the hydrating medium to obtain the best possible results. As pointed out above, Kirpotin's method involves removal of the organic solvent before the hydration.

Papahadjopoulos discloses methods of formation of liposomes. The methods involve either removal of the organic solvent before hydration (Example 1) or making an emulsion using an organic solvent containing phospholipid and an aqueous medium and evaporating the organic solvent (Example 2). In either method, the amount of the lipid is 100 micromoles and the aqueous medium added is 1.5 ml which correspond to 15 ml of aqueous medium per millimole of the phospholipid and the hydration medium contains histidine.

Making an emulsion of the phospholipid containing organic solvent and an aqueous medium in the ratios of 1 millimole of lipid/15ml of aqueous medium and removing the organic solvent to form liposomes would have been obvious to one of ordinary skill in the art since Papahadjopoulos teaches that liposomes can be produced by either process.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that Kirpotin does not teach or suggest a process for the manufacture of long circulating non-PEGylated liposomes as set forth in claim 1 and that the examiner has offered no factual evidence to support his statement that Kirpotin teaches

or suggests non-PEGylated liposomes. This argument is not persuasive since as pointed out above, although in the examples Kirpotin uses PEG-phospholipids, on col. 9, lines 22-33 teaches either the naturally occurring or synthetic phospholipids which implies that the use of PEG-phospholipids for the method of preparation of liposomes is not necessary. Applicant further argues based on the declaration by MR. Annappa that instant invention provides unexpected results compared to the PEGylated liposomal preparation (CAELYX) marketed currently. These arguments are not persuasive since the proper comparison to show unexpected results would be the comparison with Kirpotin and not with the commercially available PEGylated product since this product was not used in the rejection. Instant claims recite a process of preparation of liposomes containing phospholipids and sterol, which are not PEGylated and Kirpotin, teaches the preparation of non-PEGylated liposomes. Furthermore, instant claims are drawn to a process of preparation and the product formed and not drawn to method of increasing the circulation time of the liposomes. The examiner thus, has not merely dismissed the declarations.

5. Claims 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kirpotin (6,110,491) and Papahadjopoulos (4,235,871) in further combination with Emanuel (US 2002/0151508).

The teachings of Kirpotin and Papahadjopoulos have been discussed above. What is lacking in Kirpotin is the use of sucrose- histidine buffer. Papahadjopoulos teaches the use of histidine buffer. The use of this buffer containing even sucrose however, would have been obvious to one of ordinary skill in the art with the expectation

of obtaining similar results since the reference of Emanuel shows routine use of ammonium sulfate- histidine-sucorse buffer in the preparation of liposomes (0033 and claims 4 and 5).

Applicant's arguments although moot in view of the new rejection containing Papahadjopoulos, the examiner would address applican's arguments regarding Kirpotin and Emanuel. The examiner has already addressed applicant's arguments regarding Kirportin. Applicant argues that in Emanuel, histidine and sucrose are part of pegylated liposomes. The examiner points out once again that instant claims are drawn to a method of preparation of liposomes and Kirportin teaches that the liposomes can be prepared even without the presence of PEG.

6. Claims 1-8, 10, 12, 14-22 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forssen (5,714,163) in combination with Papahadjopoulos (4,235,871) and Janoff (4,880,635).

Forssen discloses a method of preparation of liposomes wherein the lipid film is hydrated with ammonium sulfate. The liposomes contain DSPC and cholesterol and vincristine. Vincristine is added to the preformed liposomes (Example 1) Although Forssen teaches the use of 300 mM sucrose, he does not teach the use of hydration buffer containing both ammonium sulfate and sucrose. What is lacking in Forssen is the method of preparation of liposomes first forming an emulsion of the organic solvent and an aqueous medium and the removal of the organic solvent. Also lacking is the claimed amount of the hydrating medium per millimole of phospholipid.

Papahadjopoulos discloses methods of formation of liposomes. The methods involve either removal of the organic solvent before hydration (Example 1) or making an emulsion using an organic solvent containing phospholipid and an aqueous medium and evaporating the organic solvent (Example 2). In either method, the amount of the lipid is 100 micromoles and the aqueous medium added is 1.5 ml which correspond to 15 ml of aqueous medium per millimole of the phospholipid.

Janoff teaches that sugars such as sucrose when present both inside and outside would enable the liposomes to retain Adriamycin during dehydration and rehydration (col. 21, line 23 through col. 21, line 27). Janoff further teaches the hydration of the 80 micromoles of lipid with 2 ml of buffer (25 ml per mmole).

To include sucrose in the hydration medium of Forssen would have been obvious to one of ordinary skill in the art since such a procedure would enable the presence of sucrose within the liposomes as well as outside and since Janoff teaches that the liposomes retain the active agent during dehydration and rehydration procedures. Making an emulsion of the phospholipid containing organic solvent and an aqueous medium in the ratios of 1 millimole of lipid/15ml of aqueous medium and removing the organic solvent to form liposomes would have been obvious to one of ordinary skill in the art since Papahadjopoulos teaches that liposomes can be produced by either process. Although Forssen does not specifically teach the amount of aqueous medium added per mol phospholipids, since the final product in Forssen is a liposome just as in instant case, and since the bilayer formation is a result of the complete hydration of the phospholipid, in the absence of showing unexpected results, it is deemed obvious to

one of ordinary skill in the art to vary the amounts of the hydrating medium to obtain the best possible results. One of ordinary skill in the art would be motivated to use claimed amounts of aqueous medium with the expectation of obtaining similar results since both Janoff and Papahadjopoulos teach such a hydration amount. The criticality of the histidine buffer in claim 62 is not readily apparent to the examiner since Pahapadjopoulos teaches the routine use of histidine buffer in the hydration medium.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that one skilled in the art would not be motivated to even consider Forssen or Janoff for suggesting a nonpegylated liposome made by reducing the amount of hydration buffer. This argument is not persuasive since the formation of a bilayer occurs only when the lipid film is hydrated fully and applicant has not shown through studies that the claimed amounts of hydration buffer are critical. In addition, Janoff teaches instant amounts. Furthermore, whether the liposome has a long circulation also depends upon the type of phospholipid used. Applicant has not shown that because of these hydration buffer amounts, the liposomes have the longer circulating times. The examiner cites the references of Maruyama (International Journal of Pharmaceutics) and that of Park which teaches liposome made of some negatively charged phospholipids prolong the circulation time. Applicant's arguments that Janoff teaches liposomes that are required to be dehydrated and then rehydrated to achieve long term storage are not persuasive since Janoff first of all teaches the inclusion of sugar in the hydration buffer as evident from col. 8, lines 40-43. Secondly, Janoff is combined for this teaching alone and instant 'comprising' does not exclude further

dehydration and rehydration of the liposomes. teaches liposomes which Applicant's arguments once again are based on the declaration by Mr. Annappa to show unexpected results. As pointed out above, since the rejection is based on the Forssen and Janoff and not based on the commercially available product CAELYX, the proper comparison would be with the applied prior art teachings. The rejection therefore, is maintained.

7. Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Forssen (5,714,163) in combination with Papahadjopoulos (4,235,871) and Janoff (4,880,635) as set forth above, further in view of Emanuel (US 2002/0151508).

The teachings of Forssen and Janoff have been discussed above. What is lacking in these references is the use of sucrose- histidine buffer. The use of this buffer however, would have been obvious to one of ordinary skill in the art with the expectation of obtaining similar results since the reference of Emanuel shows its routine use in the preparation of liposomes (0033 and claims 4 and 5).

8. Claims 1-8, 10-22 and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forssen (5,714,163) in combination with Papahadjopoulos (4,235,871) and Janoff (4,880,635) as set forth above, further in view of Radhakrishnan (5,192,528) or Uchiyama (International Journal of Pharmaceutics, 1995).

The teachings of Forssen and Janoff have been discussed above. As pointed out above, Forssen does not teach the hydration buffer amount to be 10 to 35 ml per mmole of the phospholipid.

Radhakrishnan while disclosing corticosteroid containing liposomes teaches that the aqueous medium is added to a final lipid concentration of between about 10 to 100 micromole/ml which translates to 100 to 10 ml per mmole phospholipid (abstract and col. 5, lines 15-29).

Uchiyama while disclosing a method of preparation of liposomes containing EPC, HEPC, DCP and cholesterol teaches the hydration of 200 micromoles of lipids using 5 ml of aqueous medium, which translates to 1 mmole lipid and 25 ml of aqueous medium (Materials and methods, liposome preparation).

It would have been obvious to one of ordinary skill in the art to use claimed amounts of the hydration medium to hydrate the lipid of Forssen since the references of Radhakrishnan and Uchiyama teach that these are typical amounts of the hydration medium.

9. Claims 1-8, 10, 12, 14-22 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hong (Clinical Cancer Research, 1999) of record in view of Papahadjopoulos (4,235,871) and Janoff cited above

Hong teaches a method of preparation of doxorubicin loaded liposomes. The method involves hydration of the lipids using ammonium sulfate solution (abstract and Materials and Methods). What is lacking in Hong is the use of sucrose in the hydration buffer. It is unclear from Hong as to how much hydration buffer is added.

Papahadjopoulos discloses methods of formation of liposomes. The methods involve either removal of the organic solvent before hydration (Example 1) or making an emulsion using an organic solvent containing phospholipid and an aqueous medium

and evaporating the organic solvent (Example 2). In either method, the amount of the lipid is 100 micromoles and the aqueous medium added is 1.5 ml which correspond to 15 ml of aqueous medium per millimole of the phospholipid.

Janoff teaches that sugars such as sucrose when present both inside and outside would enable the liposomes to retain Adriamycin during dehydration and rehydration (Example 1; col. 21, line 23 through col. 21, line 27). Janoff further teaches the hydration of the 80 micromoles of lipid with 2 ml of buffer (25 ml per mmole).

Making an emulsion of the phospholipid containing organic solvent and an aqueous medium in the ratios of 1 millimole of lipid/15ml of aqueous medium and removing the organic solvent to form liposomes would have been obvious to one of ordinary skill in the art since Papahadjopoulos teaches that liposomes can be produced by either process. To include sucrose in the hydration medium of Forssen would have been obvious to one of ordinary skill in the art since such a procedure would enable the presence of sucrose within the liposomes as well as outside and since Janoff teaches that the liposomes retain the active agent during dehydration and rehydration procedures.

Although applicant's arguments are deemed to be moot, the examiner would address applicant's arguments with regard to Hong and Janoff. Applicant argues that Hong is directed to the preparation of both pegylated liposomes. This argument is not persuasive since Hong teaches the preparation of both liposomal composition with and without PEG as the title in Hong itself states (see also Materials and Methods and

Figures 1-4). Instant claims are method of preparation and product claims. The motivation to add ammonium sulfate and sucrose need not be the same as applicant's.

Applicant argues the following with regard to Janoff:

"First, the abstract of Janoff provides the gist ot the Janoff process. The very first sentence is: "Dehydrated liposomes are prepared by drying liposome preparations under reduced pressure in the presence of one or more protective sugars, e.g., the disaccharides, trehalose and sucrose." This indicates that Janoff does not disclose hydration of phospholipids to form liposomes using sugar in the hydration medium as Janoff is concerned with rehydrating dehydrated liposomes. Protective sugars are used while drying liposome preparations under reduced pressure. Further the protective sugar can be omitted if: (1) the liposomes are the type which have multiple lipid layers; (2) the dehydration is preferred without prior freezing; and (3) the dehydration is performed to an end point that results in sufficient water left in the preparation (e.g. at least 12 moles water/mole lipid). In the process of claim 1 of the present application, at the stage of hydration of phospholipids, all the three conditions exists and thus, according to Janoff, addition of sugar is not necessary. Second, Janoff's hydration medium for hydrating dehydrated liposomes contains NaC1 and HEPES containing sugar. In contrast, the claimed hydration medium contains ammonium sulfate and sucrose for hydrating phospholipids. Applicants submit that the use of NaC1 and Hepes does not teach or suggest the use of ammonium sulfate and sucrose in the method of hydration of phospholipids. The Examiner provides no reason why one of ordinary skill in the art would have been motivated to look to a reference that teaches NaC1 and HEPES for hydrating dehydrated liposomes to arrive at using ammonium sulfate for hydrating phospholipids. Further, the use of a hydration medium is not independent of the quality of the hydration medium's composition. How does the Examiner make the leap that a reference teaching NaC1/Hepes/sugar rehydration buffer used to rehydrate dehydrated liposomes teaches or suggests ammonium sulfate/sucrose hydration buffer used to hydrate phospholipids at the recited ratio? Applicants contend that such a stark difference in the composition an____d the reasons for use of the Janoff medium and the hydration medium of the present invention further illustrates why one of ordinary skill would have never even considered Janoff, much less be motivated by Janoff to combine its teachings as suggested by the Examiner to arrive at a process of preparing liposomes as recited in claim 1 (i.e., a process of preparing long circulating liposomes, incorporating ammonium sulfate and sucrose in limited defined amounts of hydration medium). Third, Janoff teaches liposomes that are required to be dehydrated and then rehydrated to achieve long-term storage without substantial loss of their internal contents. Janoff does not teach or suggest that the addition of sugar in the hydration media along with ammonium sulfate for hydrating phospholipids in the preparation of liposomes is required (as required by the present claims), in a certain ratio and in combination with the recited phosphatidyl cholines to achieve a long-circulating liposome. Fourth, applicants submit that Janoff does not even teach using sucrose in a hydration buffer when dehydration/rehydration is not necessary. Put another way, one of ordinary skill would not have been motivated to even consider using just one of these recited elements (i.e. use of sucrose with ammonium sulfate in the hydration buffer) in the Janoff process because, according to Janoff, when there is no dehydration step (as in the present pending claim 1), there is no need for rehydration and therefore no need for a protective sugar. See Janoff abstract stating how much

dehydration is necessary to incorporate sugar in the rehydration medium for rehydration of dehydrated liposomes. Thus, the method of hydration of phospholipids using sucrose in the medium to create liposome is not at all obvious from Janoff. In this way, Janoff effectively teaches away from the use of sugar in the hydration medium when dehydration is not necessary, as is the case in claim 1, where the liposomes formed are in abundant water. Janoff does not teach or suggest all the elements of the present claims nor teach the liposome produced by the claimed method."

These arguments are nor persuasive since in Example 1, Janoff clearly teaches the dehydration of liposomes using protective sugar trehalose. This implies the protection of the sugar, sucrose (col. 5, line 60) during dehydration process of the liposomes (see also col. 7, lines 47-61).

9. Claims 1-8, 10, 12, 14-22 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hong (Clinical Cancer Research, 1999) of record in view of Papahadjopoulos (4,235,871) and Janoff cited above
and either Radhakrishnan (5,192,528) or Uchiyama cited above.

Hong teaches a method of preparation of doxorubicin loaded liposomes. The method involves hydration of the lipids using ammonium sulfate solution (abstract and Materials and Methods). What is lacking in Hong is the use of sucrose in the hydration buffer. It is unclear from Hong as to how much hydration buffer is added.

Papahadjopoulos discloses methods of formation of liposomes. The methods involve either removal of the organic solvent before hydration (Example 1) or making an emulsion using an organic solvent containing phospholipid and an aqueous medium and evaporating the organic solvent (Example 2). In either method, the amount of the lipid is 100 micromoles and the aqueous medium added is 1.5 ml which correspond to

15 ml of aqueous medium per millimole of the phospholipid and the hydration medium contains histidine.

Janoff teaches that sugars such as sucrose when present both inside and outside would enable the liposomes to retain Adriamycin during dehydration and rehydration (col. 21, line 23 through col. 21, line 27). Janoff further teaches the hydration of the 80 micromoles of lipid with 2 ml of buffer (25 ml per mmole).

Radhakrishnan while disclosing corticosteroid containing liposomes teaches that the aqueous medium is added to a final lipid concentration of between about 10 to 100 micromole/ml which translates to 100 to 10 ml per mmole phospholipid (abstract and col. 5, lines 15-29).

Uchiyama while disclosing a method of preparation of liposomes containing EPC, HEPC, DCP and cholesterol teaches the hydration of 200 micromoles of lipids using 5 ml of aqueous medium, which translates to 1 mmole lipid and 25 ml of aqueous medium (Materials and methods, liposome preparation).

One of ordinary skill in the art would be motivated to use claimed amounts for the hydration medium since the references of Radhakrishnan and Uchiyama show the routine use of claimed amounts for hydrating the phospholipids to form liposomes. .

10. Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hong (Clinical Cancer Research, 1999) of record in view of Papahadjopoulos (4,235,871) Janoff cited above and either Radhakrishnan (5,192,528) or Uchiyama cited above, further in view of Emanuel (US 2002/0151508).

The teachings of Hong, Papahadjopoulos, Janoff and Radhakrishnan have been discussed above. What is lacking in these references is the use of sucrose- histidine buffer. The use of this buffer however, would have been obvious to one of ordinary skill in the art with the expectation of obtaining similar results since the reference of Emanuel shows its routine use in the preparation of liposomes (0033 and claims 4 and 5).

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

GSK